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RESEARCH ARTICLE

The Prevalence and Distribution of High Risk Human Papillomavirus Genotypes in Patients with Dysplastic Lesions: a Population Study

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Background. Cervical cancer (CC) is a major public health problem worldwide. Knowledge of human papillomavirus (HPV) genotype prevalence and distribution is important for the introduction of an effective vaccination program and the corresponding epidemiological monitoring. The aim of this study was to identify and analyze the distribution of high-risk HPV genotypes. **Methods**. Data were collected from 136 patients for the detection of circulating HPV genotypes, where Pap test results revealed the presence of koilocytes or high risk (HR) dysplastic lesions, elements that raise the suspicion of HPV infection. **Results**. HPV infection was identified in 72 (55.4%) of the patients tested, 34 (47.3%) with single infection, and 38 (52.7%) with multiple infections. Twenty-two different types of HPV were identified: 14 high risk HPV types, 7 low risk HPV types, 1 probable high risk HPV type. HPV 16 was the most frequently detected (55.6%) one, it was involved in single (15 cases) and multiple (25 cases) infections, primarily associated with type 18 (12 cases), and type 52 (11 cases). The presence of HPV 18 (29.2%) and HPV 52 (23.6%) was identified after HPV type 16. **Conclusions**. Oncogenic HPV genotypes 16, 18, and 52 were most frequently associated in women with dysplastic lesions, which require the use of polyvalent HPV vaccines when assessing cross-protective effects of specific immunoprophylaxis programs.

Keywords: Human papillomavirus, cervical cancer, HPV genotype

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Introduction

Cervical cancer (CC) is a major public health problem worldwide. It is the fourth most common cancer in women, representing 8.8% of all cancers, with an incidence rate estimated at 560,000 cases in 2015. It is expected that about 460,000 women aged 65 will be affected. About 266,000 deaths are recorded yearly due to cervical cancer, representing 7.5% of all cancer deaths in women. The mortality rate is continuously increasing by about 190,000 cases identified in women under the age of 65 years [1,2].

Romania ranks first in Europe in terms of CC mortality ($10.77\%_{000}$), 6.3 times higher than the mean in European Union countries. Of all cancers in women in Romania, CC ranks 4 in terms of mortality rate. The highest mortality rates were found in age groups 50-60 years ($32.9\%_{000}$), 60-70 years ($37.3\%_{000}$), 70-80 years ($38.5\%_{000}$). The incidence rate was an estimated $28.65\%_{000}$, with 4,000 new cases discovered according to data from 2012, ranking this cancer the third. The highest incidence rates were found in age groups 50-60 years ($82.1\%_{000}$), 60-70 years ($69.0\%_{000}$), 40-50 years ($60.1\%_{000}$) [2].

Human papillomavirus (HPV) infection is associated with 99.7% of CCs, and it is considered a necessary cause for the occurrence of this type of cancer [3,4].

To date, 176 types of HPV have been identified isolated from different areas of the body. These types have been collected in two databases (http://pave.niaid.nih.gov, http://www.hpvcenter.se), but their number is growing, depending on new isolation techniques [5-8].

HPV genotypes are divided into two classes: high risk (cancer-causing), and low risk, 40 of which are known to infect the anogenital mucosa. Fifteen oncogenic strains of HPV associated with pre-cancerous lesions (intraepithelial with high risk) or CC have been identified (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82). Research shows that oncogenic HPV strains 16 and 18 cause about 70% of CCs worldwide. About 10% of all CC cases are caused by HPV 45, and HPV 31. A probable oncogenic risk is assigned to genotype 26, while possible oncogenic risk is assigned to the following types: HPV 53, 66, 67, 70, 30, 34, 69, 85, and 97. Low risk genotypes are: HPV 6, 11, 28, 32, 40, 42, 43, 44, 54, 55, 57, 61, 62, 71, 72, 74, 81, 83, 84, 86, 87, and 89. Low risk strains can cause benign anogenital vegetation or low risk intraepithelial lesions, these types not being associated with any type of pre-cancerous lesions [9,10].

Despite the medical importance and high incidence rate of CC, there are few studies about the Romanian population regarding HPV genotype distribution circulating in the population [11-13].

Given the interest in preventing CC, it is very important to check the prevalence of different types of HPV, especially the high risk ones. Moreover, it is also important to investigate whether different groups of women have adequate knowledge and perceive their behavior as risky for infection with HPV, in order to provide them with appropriate and useful information. By identifying the predomi-

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nant circulating HPV genotypes, and the incidence of infection with oncogenic HPV types, a report on accurate information for specialists regarding the situation could be prepared in order to influence subsequent behavior towards HPV vaccination: establishing the necessary amount of HPV vaccine, target groups where the vaccine would have maximum efficacy, the percentage of the people who should be vaccinated, the influence of future vaccination campaigns, etc.

Aim of the study: to identify and analyze the distribution of high risk HPV genotypes present in women where Pap test results revealed the presence of koilocytes or dysplastic LSIL (Low Grade Squamous Intraepithelial Lesion), and HSIL (High Grade Squamous Intraepithelial Lesion) type lesions, features that raise the suspicion of HPV infection.

Materials and methods

Target population

We used a cross-sectional study to identify population groups at high risk for HPV infection in Mureş County, Romania, between June 2014 and March 2015, groups which would require HPV vaccination. Mureş County is located in the Central Region of the country with a population of about 500,000 inhabitants, 54.5% of which are female [14]. The target population was represented by patients who sought specialist examination in two private gynecological surgeries specialized in CC pathology, with an average of four patients with cervical diseases consulted per week. Pap test results revealed the presence of koilocytes or LSIL and HSIL dysplastic lesions, features that raise the suspicion of HPV infection. Samples were collected from these patients to detect circulating HPV genotypes. Each patient received an additional questionnaire that requested information on demographics, sexual behavior, and awareness about HPV infection and HPV vaccination. The data from the questionnaires were correlated with results obtained by genotyping. Copies of the questionnaire (in Romanian) are available from the authors. The study was approved by the Ethics Committee of the University of Medicine and Pharmacy of Tîrgu Mureş.

Data collection

Cytological samples were collected with a cervical brush on Cobas PCR Cell Collection (Roche) culture medium by a gynecologist. After collecting, the samples were stored at 4°C, then transferred to and processed in the Central Laboratory of the Emergency County Hospital of Tîrgu Mureş, Mureş County. Additional information was obtained from each patient and collected in a table (initials, age, presence of koilocytes, type of dysplastic lesion, type of genotype). Applying the Bethesda System, the cytology results were classified into: NILM (Negative for Intraepithelial Lesions or Malignancy), ASCUS (Atypical Squamous Cells of Undetermined Significance), ASCH (Atypical Squamous Cells for which the High-grade lesion cannot be excluded), LSIL, and HSIL.

DNA extraction and HPV DNA detection

The specimen preparation using the AmpliLute Liquid Media Extraction Kit yields HPV target DNA and human genomic DNA suitable for PCR amplification, according to the manufacturer's guidelines. The Master Mix reagent contains primers for the amplification of DNA from 37 HPV genotypes and the human β-globin gene. The detection and genotype determination is performed using the denatured amplified DNA and an array of oligonucleotide probes that permit independent identification of individual HPV genotypes.

The LINEAR ARRAY HPV Genotyping Test uses biotinylated primers to define a sequence of nucleotides within the polymorphic L1 region of the HPV genome that is approximately 450 base pairs long. A pool of HPV primers present in the Master Mix is designed to amplify HPV DNA from 37 HPV genotypes including 13 high risk gen-

Table I. Demographics, sexual behavior, attitudes towards preventing HPV infection

Characteristics	Number of women, no (%) 130 (100%)
Age, mean ± SD (range)	39.5±10.6 (19-61)
Education, no (%)	
Primary	24 (18.4)
High school	43 (33.1)
Post-secondary education	26 (20.0)
University degree	33 (25.4)
Post-graduate studies	4 (33.1)
Marital status, no (%)	
Unmarried	19 (14.6)
Married	68 (52.2)
Widowed	11 (8.5)
Divorced	21 (16.2)
Concubinage	11 (8.5)
Menarche-years, mean ± SD (range)	13.5±1.2 (11-17)
First sexual intercourse-years, mean ± SD (range)	18.4±2.1 (14-28)
Type of sexual intercourse, no (%)	
Vaginal	130 (100.0)
Anal	7 (5.4)
Oral	22 (16.9)
Do you have a stable sexual partner? no (%)	
No	28 (21.5)
Yes	102 (78.5)
How many sexual partners have you had so far?, no (%)	34 (26.2)
One,	73 (56.2)
2-4,	16 (12.2)
5-9,	7 (5.4)
Over 10	
Duration of sexual activity, no (%)	
Under 10 years	27 (20.8)
11-20 years	39 (30.0)
Over 21 de years	64 (49.2)
The frequency of sexual intercourses per week (average), no (%)	
1-2,	110 (84.6)
3-4,	9 (6.9)
Over 5	11 (8.5)
Have you heard of HPV infection?, no (%)	
Yes	97 (74.6)
No	33 (25.4)
How many times have you been tested by cervical Pap smear?, no (%)	
Never	23 (17.7)
2-3 times	56 (43.1)
over 3 times	51 (39.2)

otypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68). Capture probe sequences are located in polymorphic regions of L1 bound by these primers. An additional primer pair targets the human B-globin gene to provide a control for cell adequacy, extraction and amplification.

Statistical analysis

Statistical analysis was Performed Using MedCalc Software (bvba Version 12.3.0, Mariakerke, Belgium). Student test was used to assess differences in the means of continuous variables - patient age (mean ± SD), while χ^2 test, Z test or Fisher's exact test were used for categorical variables (expressed by number (%). All tests were interpreted in relation to p=0.05 and statistical significance was considered for p-values under the significance threshold.

Results

Data were collected from 136 patients in whom the presence of koilocytes or LSIL and HSIL dysplastic lesions was identified. By performing genotyping, 6 samples were inadequate and were excluded. Thus, statistical analysis was performed on 130 patients. Socio-demographic characteristics, namely those related to sexual behavior, are shown in Table I.

HPV type-specific prevalence

HPV infection has been identified in 72 (55.4%) of the patients tested, 34 (47.3%) with single and 38 (52.7%) with multiple infections (Table II). In women free of infection we found a mean age of 37.4 ± 8.3 years, significantly lower than in women with single (42.1 ± 12.5 years) or with multiple infections (40.4 ± 11.5 years). We identified 22 different types of HPV: 14 high risk types, 7 low risk types, and 1 type possible high risk HPV. High risk HPV type 16 was the most frequently detected (55.6%). HPV 16 was involved in single (15 cases) and multiple (25 cases) infections, primarily associated with type 18 (12 cases) and type 52 (11 cases). The presence of types 18 (29.2%) and 52 (23.6%) was also observed. Of the multiple HPV infections (38 patients) various combinations were detected: two (65.8%), three (15.8 %), four (15.8%), or six (2.6%). Only in the case of multiple infections, not in the single ones, were the following HPV genotypes isolated: high risk – 33, 35, 39, 45, 51, 58, 59, 82; low risk – 6, 55, 81.

Cytological examination showed the following results: ASCH (22/130-16.9%; CI95%: 11.4-24.3), ASCUS (20/130-15.4%; CI95%: 10.2-22.5), H-SIL (25/130-19.2%; CI95%: 13.4-26.8), L-SIL (40/130-30.8%; CI95%: 23.5-39.1), NILM (23/130-17.7%; CI95%: 12.1-25.1), (Table III).

Of the women with positive HPV types, HR-HPV were identified in 63 (87.5%), and depending on cytology results in different percentages: ASCH (6-9.5%; CI95%: 4.4-19.2), ASCUS (6-9.5%; CI95%: 4.4-19.2), H-SIL (20-31.7%; CI95%: 21.6-44.1), L-SIL (19-30.2%; CI95%: 20.2-42.4), NILM (12-19.1%; CI95%: 11.2-30.4).

LR-HPV types were identified in nine (12.5%) women, and depending on cytology results in different percentages: ASCH (2-22.2%; CI95%: 6.3-54.7), ASCUS (1-11.1%; CI95%: 1.9-43.5), H-SIL (0-0.0%; CI95%: 0-29.9), L-SIL (3-33.3%; CI95%: 12.1-64.5), NILM (3-33.3%; CI95%: 12.1-64.5). Table III shows the associations of the most common genotypes identified in our study group, as well as the cytological aspects.

We recorded the sexual behavior of the patients with the most common genotypes, thus the used statistical tests

Table II. Distribution of HPV genotypes (% [95% confidence interval]) in women with single infection cervical dysplasia or multiple infections with different types of HPV

Genotype	Risk HPV*	Single infection 34 (47.2%)	Multiple infection 38 (52.8%)	Positive HPV 72 (55.4%)	P value*
16	HR	44.1 (27.4-60.8)	65.8 (50.7-80.9)	55.6 (44.1-67.0)	0.10
18	HR	20.6 (7.0-34.2)	36.8 (21.5-52.2)	29.2 (18.7-39.7)	0.21
52	HR	5.9 (2.0-13.8)	39.5 (23.9-55.0)	23.6 (13.8-33.4)	0.002
31	HR	11.8 (9.0-22.6)	7.9 (5.0-16.5)	9.7 (2.9-16.6)	0.87
33	HR	0.0 (0-4.5)	15.8 (6.2-27.4)	8.3 (1.9-14.7)	0.04
35	HR	0.0 (0-4.5)	15.8 (6.2-27.4)	8.3 (1.9-14.7)	0.04
61	LR	2.9 (1.7-8.6)	10.5 (5.9-20.3)	6.9 (1.1-12.8)	0.42
42	LR	2.9 (1.7-8.6)	7.9 (5.0-16.5)	5.6 (0.3-10.8)	0.68
62	LR	0.0 (0-4.5)	10.5 (5.9-20.3)	5.6 (0.3-10.8)	0.15
68	HR	2.9 (1.7-8.6)	5.3 (2.8-12.4)	4.2 (0.2-8.8)	0.93
58	HR	0.0 (0-4.5)	7.9 (5.0-16.5)	4.2 (0.2-8.8)	0.27
51	HR	0.0 (0-4.5)	5.3 (2.8-12.4)	2.8 (0.1-6.6)	0.51
53	PHR	2.9 (1.7-8.6)	2.6 (1.4-7.7)	2.8 (0.1-6.6)	0.52
81	LR	0.0 (0-4.5)	5.3 (2.8-12.4)	2.8 (0.1-6.6)	0.51
82	HR	0.0 (0-4.5)	5.3 (2.8-12.4)	2.8 (0.1-6.6)	0.51
6	LR	0.0 (0-4.5)	2.6 (1.4-7.7)	1.4 (0.1-4.1)	0.94
32	LR	2.9 (1.7-8.6)	0.0 (0-5.4)	1.4 (0.1-4.1)	0.96
39	HR	0.0 (0-4.5)	2.6 (1.4-7.7)	1.4 (0.1-4.1)	0.94
45	HR	0.0 (0-4.5)	2.6 (1.4-7.7)	1.4 (0.1-4.1)	0.94
55	LR	0.0 (0-4.5)	2.6 (1.4-7.7)	1.4 (0.1-4.1)	0.94
56	HR	2.9 (1.7-8.6)	0.0 (0-5.4)	1.4 (0.1-4.1)	0.96
59	HR	0.0 (0-4.5)	2.6 (1.4-7.7)	1.4 (0.1-4.1)	0.94

*HR-high risk, PHR-probable high risk, LR-low risk; ** Single infection versus multiple infection, Z-test or Fisher' s exact test.

Table III. Prevalence of HPV types in women with normal and abnormal cytological results according to the most common genotypes

	All HPV 72 (100%)	HPV 16 40 (55.6%)	CI 95%	HPV 18 21 (29.2%)	CI 95%	HPV 52 17 (23.6%)	CI 95%
Age, mean±SD	41.2±11.9	44.1±12.2	-	44.3±15.6	-	42.4±7.7	-
ASCH, 22 (16.9%)	8 (11.1)	4 (10.0)	3.9-23.1	0 (0.0)	0-15.4	4 (23.5)	9.5-47.2
ASCUS, 20 (15.4%)	7 (9.7)	1 (2.5)	0.4-12.8	1 (4.7)	0.8-22.6	0 (0.0)	0.0-18.4
L-SIL, 40 (30.8%)	22 (30.6)	4 (10.0)	3.9-23.1	10 (47.6)	28.3-67.6	3 (17.6)	6.2-41.1
H-SIL, 25 (19.2%)	20 (27.8)	20 (50.0)	35.0-64.8	7 (33.3)	17.2-54.6	5 (29.4)	13.2-53.1
NILM, 23 (17.7%)	15 (20.8)	11 (27.5)	16.1-42.8	3 (14.3)	4.9-34.6	5 (29.4)	13.2-53.1
Single HPV infection	34 (47.3)	15 (37.5)	24.2-52.9	7 (33.6)	17.2-54.6	2 (11.7)	3.3-34.3
HPV co-infection	38 (52.7)	25 (62.5)	47.1-75.7	14 (66.6)	45.3-82.8	15 (88.2)	65.6-96.7

identified statistical significance only in relation to the frequency of performing the Pap smear test (Table IV).

Discussions

This study provides information on the prevalence of HPV infection and the distribution of specific genotypes circulating among women who presented to a specialist and in whom examinations revealed dysplastic lesions. Our data have shown an increased prevalence of HPV infection, 55.4% of patients with suspected lesions through cervical Pap smear. The risk of CC increases along with the incidence of some HPV genotypes. Our results demonstrated the predominance of HPV genotypes 16 (55.6%), followed by HPV types 18 (29.2%), and 52 (23.6%). In total we found 22 different genotypes, 63.6% of them with high oncogenic risk. In approximately 47% of the patients we identified a single genotype HPV infection, the others in co-infection with two, three, four, or six genotypes. Genotype HPV 16 was frequently detected in single infections, on the other hand HPV genotypes 18 and 52 mainly in associated infections. Following cytological examination, HPV genotype distribution showed that HPV 16 is commonly associated with changes in H-SIL, HPV 18 with L-SIL and H-SIL aspects, and HPV 52 with H-SIL and ASCH modifications.

Not all oncogenic HPV infections lead to CC, however, Romania ranks first in Europe in terms of mortality due to CC. The distribution of HPV genotypes in our study is similar to other regions around the country.

In a study by Ursu et al. [12] conducted on a group of women in northeastern Romania, the most common HPV genotypes were 16 (28.1%), 53 (14.6%), 51 (13.5%), 52 (10.9%), 18 (7.8 %), and 31 (7.3%). Anton et al. [13], in a study conducted for specific geographical regions of Romania, commonly identified HPV types 16 (32.6%), followed by types HPV 18, HPV 31 and HPV 51. In this study, HPV DNA was detected in 60.7% of cases and the presence of H-SIL in the cytology results was confirmed in 82.7% of cases. In a study by Moga et al. [11] the specific prevalence of HPV genotype showed more commonly HPV 16 (26%) and HPV 18 (8.58%). From the group of women investigated, 39.6% were infected with HPV, of which 42.9% with single infection, and 57.1% in various co-infections.

According to some studies conducted in Central and Eastern European countries, the prevalence of HPV/ DNA in women with HSIL was 78.1%. The prevalence of infection with oncogenic high risk HPV types was 84.2%. Prevalence of HPV types 16/18 in these women with HSIL was 61.0%, with a variation of 44.2% in Romania to 65.5% in Slovenia [15-17]. After HPV types 16, the most commonly detected types were HPV 31 and HPV 33, followed by HPV 58, 18, 45, and 56 in the Czech Republic, or HPV 58, 51, 52, and 18 in Slovenia. According to a study by

Table IV. Sexual behavior in relation to the most common genotypes

	HPV 16 40 (55.6%)	P value	HPV 18 21 (29.2%)	P value	HPV 52 17 (23.6%)	P value
What kind of sexual contact have you had?, no (%)						
Vaginal	40 (100.0%)	0.08	21 (100.0%)	0.26	17 (100.0%)	0.41
Anal	3 (7.5%)		3 (14.3%)		0 (0.0%)	
Oral	4 (10.0%)		4 (19.1%)		1 (5.9%)	
Do you have a stable sexual partner?, no (%)						
No	12 (30.0%)	0.43	8 (38.1%)	0.14	4 (23.5%)	0.76
Yes	28 (70.0%)		13 (61.9%)		13 (76.5%)	
How many sexual partners have you had so far?, no (%)						
One,	10 (25.0%)	0.68	7 (33.3%)	0.32	3 (17.6%)	0.35
2-4,	22 (55.0%)		8 (38.1%)		12 (70.6%)	
5-9,	6 (15.0%)		3 (14.3%)		2 (11.8%)	
Over 10	2 (5.0%)		3 (14.3%)		0 (0.0%)	
Have you heard about HPV infection? no (%)						
Yes	26 (65.0)	0.73	13 (61.9%)	0.58	11 (64.7)	0.84
No	14 (35.0)		8 (38.1%)		6 (35.3)	
How many times have you been tested by cervical Pap smear?, no (%)						
Never	4 (10.3%)	0.02	6 (28.8%)	0.01	1 (5.9%)	0.05
2-3 times	24 (61.5%)		13 (61.9%)		9 (52.9%)	
Over 3 times	12 (28.2%)		2 (9.5%)		7 (41.2%)	

Boumba et al. [9], the most common genotype in Europe was HPV 16, followed by HPV 18, 33, 45, 31, and in the world HPV 16, 18, 33, 45, 58.

The presence of these genotypes indicates a significant risk for developing CC. High risk genotypes HPV 16 and 18 are most commonly associated with CC, and are responsible for about two thirds of all CCs worldwide [18,19].

It is estimated that up to 80% of women will acquire an HPV infection throughout life; of such infections a ratio of up to 50% - 75% will be with one oncogenic HPV type. A woman can become infected with HPV several times in life, because natural infection does not provide protective immunity; previous HPV infection may not induce a sufficient immunity to prevent from future infections. Both young and elderly women are at risk of developing CC as a result of new infections or re-infection with one of the oncogenic HPV types [20,21]. Moreover, two HPV vaccines have been developed, a bivalent vaccine effective against genotypes HPV-16, and HPV-18, and a tetravalent vaccine against genotypes HPV-16, HPV-18, HPV-6, and HPV-11 [22,23].

Although HPV infection is the most common, it is not the only reason for developing CC. There are other demographic and behavioral risk factors that increase the relative risk of developing cancer: low education level, beginning sexual life at a young age, multiple sexual partners, long-term use of oral contraceptives, personal history of sexually transmitted infections, the presence of genital warts, lack of routine cytological screening or abnormal smears performed previously [24].

All participants in our study had begun their sexual activity, the mean age of the first sexual experience was 18.4 years, 54.6% did not use a condom at the first intercourse. Of all the positive women detected with high risk HPV, 79.2% reported use of oral contraceptives, 28.4% had associated with gynecological pathology, and 17.7% reported more than four sexual partners. Following sexual behavior in patients with the most common genotypes (HPV 16, HPV 18, and HPV 52), we found statistical significance only in relation to the frequency of Pap smear test. Probably, on a first gynecological examination, the women were diagnosed with some changes in the cervix, which is why they were recommended repeated tests.

According to some studies, in order to reduce the chances of HPV infection and related diseases, sexual partners should use condoms during every sexual intercourse, limiting the number of sexual partners, namely choosing a partner that did not have many previous sexual partners [25]. It has been shown that the HPV vaccine provides better protection than condoms; however, a vaccine-condom combination offers the best protection [26].

Another finding of the current study was the analysis of socio-demographic variables, education level and marital status were significant predictors for proven knowledge of how HPV infection is transmitted. Specifically, women who had graduate or post-secondary studies or who were married had wider knowledge versus unmarried women or those with a lower level of education. This kind of women pay increased attention to the risk of contracting a sexually transmitted disease, the sexual partner's sexual history, choosing the right contraceptive method, or the need to perform Pap cytology.

Limitations to the study: Potential methodological limitations should be considered in order to assess the results of this study. First, genotyping was done by taking samples from women with dysplastic lesions, thus, HPV genotype prevalence of such results could be overestimated compared with the general female population. However, our results were compared with epidemiological studies that investigated the prevalence of HPV genotypes in groups of women with various symptoms or genital diseases. Another limit would be the fact that the survey was based on face-to-face interviews, as such, some women may have felt uncomfortable about some questions, particularly those about sexual behavior, despite the fact that anonymity and confidentiality were guaranteed. Even with these potential limitations, the research is based on a well-designed study, a good rate of response to the questionnaire, all these features consolidating the accurate and valuable results.

Conclusions

The prevalence of HPV infection was 55% in patients with suspected lesions of the cervix following cervical Pap smear. We noticed a circulation of oncogenic HPV strains (16, 18, 52), recommending the use of polyvalent HPV vaccines when assessing the cross-protective effects of specific immunoprophylaxis programs. Our results also suggest that screening tests based on specific high risk HPV-DNA should focus on identifying HPV types 16, 18, and 52. Educational health programs focusing on raising awareness among women are needed, taking the best health decisions when dysplastic lesions are detected, which, as observed in our study, may be associated with oncogenic HPV genotypes.

Conflict of interests

The authors declare that they have no conflict of interest.

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List of acronyms

CC – Cervical cancer
HPV - Human papillomavirus
RT-PCR -Reverse transcription polymerase chain reaction

LGSIL - Low Grade Squamous Intraepithelial Lesion
HGSIL - High Grade Squamous Intraepithelial Lesion
HR-High Risk
PHR-Probable High Risk
LR-Low Risk
NILM - Negative for Intraepithelial Lesion and Malignancy
ASCUS - Atypical Squamous Cells of Undetermined Significance
ASCH - Atypical Squamous Cells for which a High-grade lesion cannot be excluded
CI - Confidence Interval

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